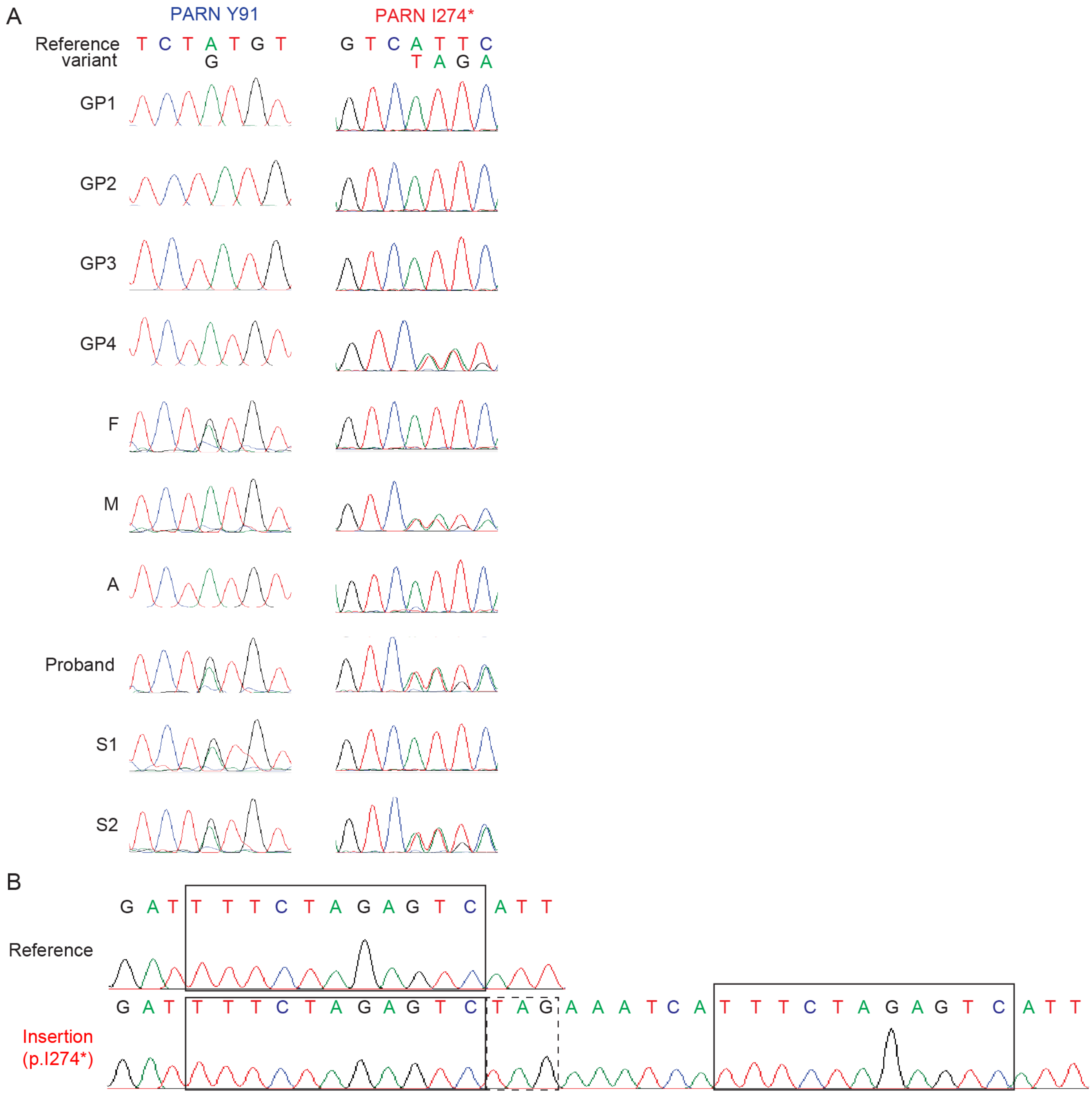
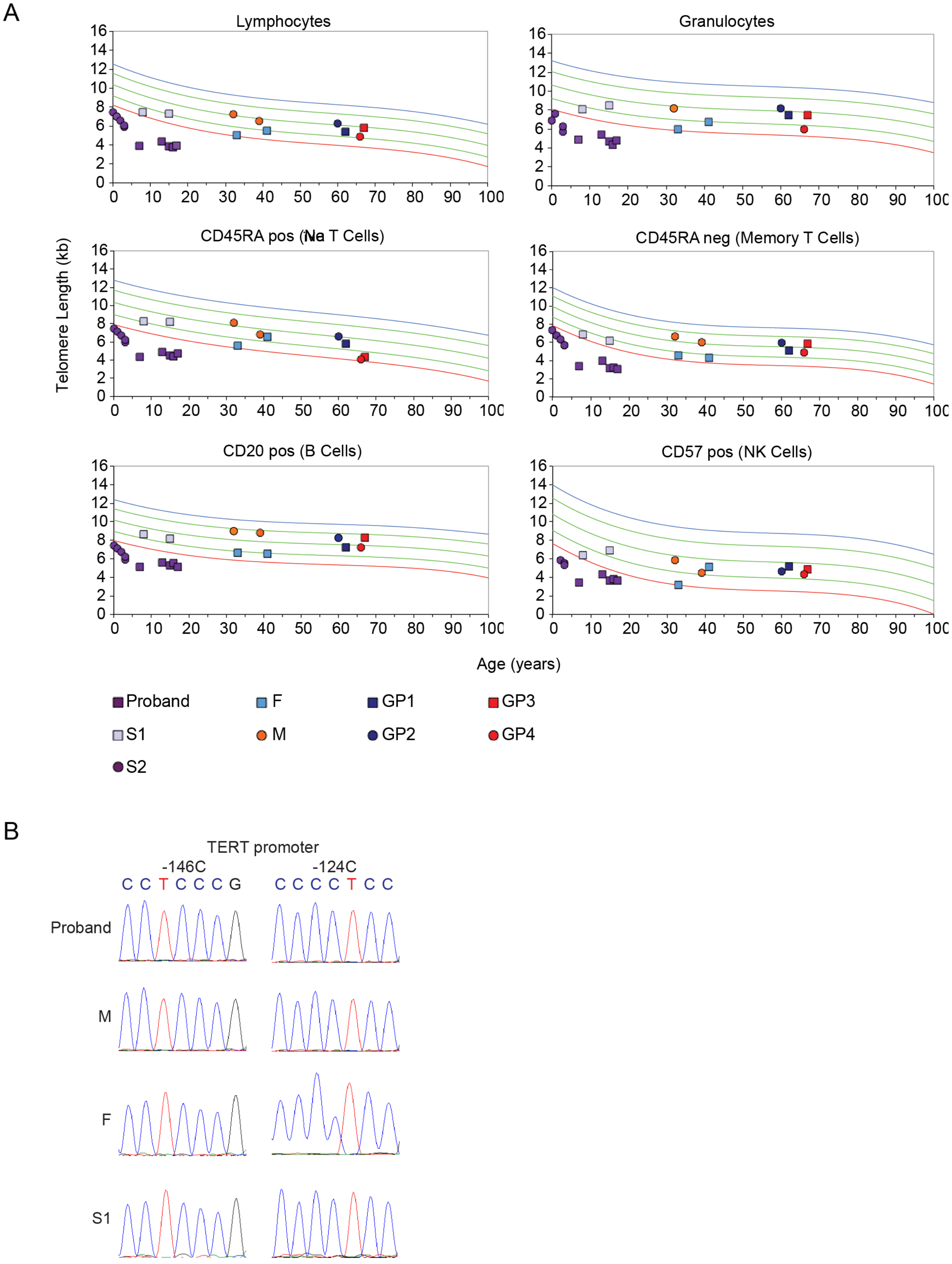
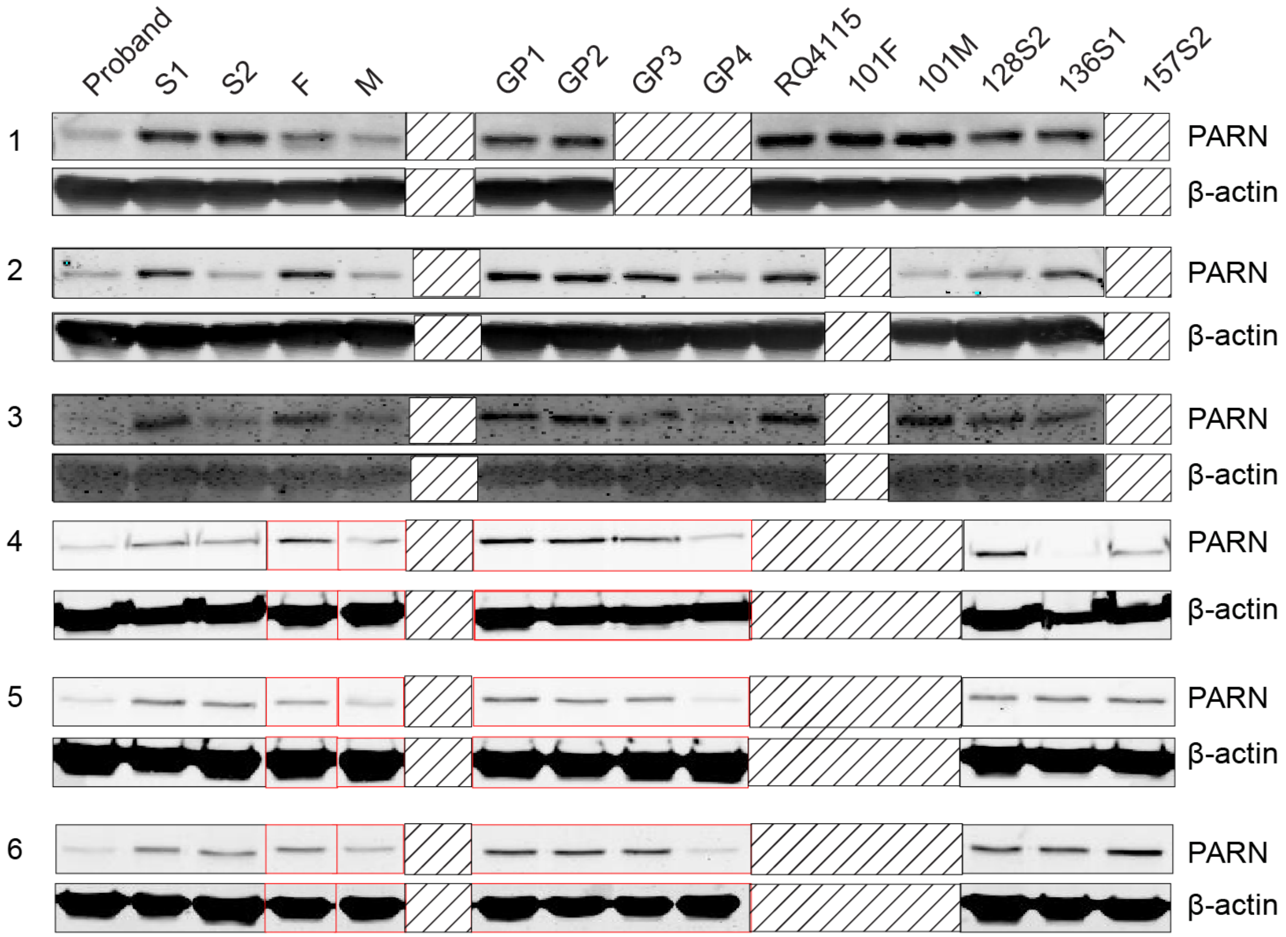
Supp. Figure S1 Cerebellar hypoplasia in BMF22 proband and S2. **(A)** T1 Sagittal MRI in BMF22 proband at 6 years of age and **(B)** younger sister S2 at 14 months of age, both demonstrate diminutive cerebellum with atrophic folia (arrows). **(C)** A normal control MRI is shown for comparison.



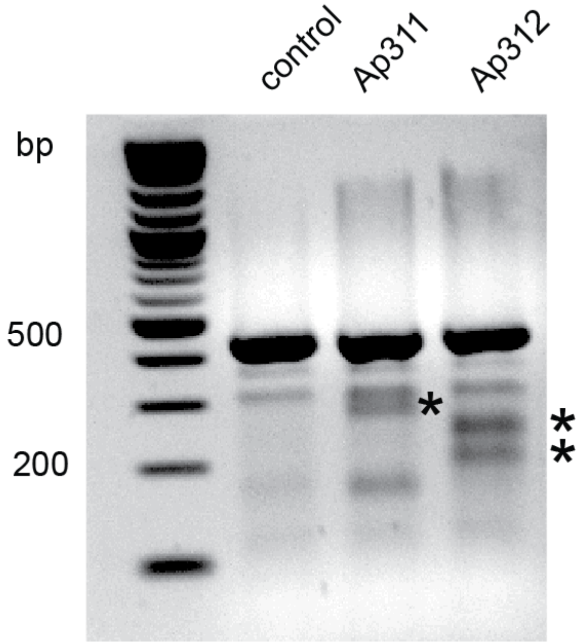
Supp. Figure S2 Inheritance of PARN NM_002582.3:p.Y91C and p.(I274*) alleles among BMF22 family members. (**A**) Sanger sequencing of peripheral blood DNA at the location of the *PARN* variants. (**B**) Sanger sequencing of each allele after TOPO cloning shows a region of microhomology in the insertion sequence.



Supp. Figure S3 Telomere flow FISH of BMF22 family members and *TERT* promoter mutation of M. **(A)** Telomere flow FISH of the granulocytes and subpopulations of lymphocytes. From top to bottom, the colored lines indicate 99th, 90th, 50th, 10th, and 1st percentile telomere lengths. (**B**) Sanger sequencing of the TERT promoter in peripheral blood DNA at locations NC_000005.10(TERT_v002):c.-146C>T.



Supp. Figure S4 PARN western blots used in addition to the western blot in Figure 3A, for the quantification of biological replicates in Figure 3B. Boxes with diagonal lines obscure samples from family members or controls for which there were only 1 or 2 samples, and were, therefore, excluded from the analysis. Red lines indicate the image is from a membrane processed in parallel.



Supp. Figure S5 Efficiency of site specific targeting of *PARN* exon 12 by sgRNAs expressed on plasmids Ap311 and Ap312 as determined using the Guide-It Mutation Detection Kit (Clontech). Control DNA from nontransfected cells. Predicated fragments indicated by asterisks.

Supp. Table S1 Penetrance in *PARN* variant carriers by gender in Stuart et al [1]. Pulmonary fibrosis or lung disease incidence by sex in the individuals reported by Stuart et al., who are 72 years or older and carry a pathogenic *PARN* variant.

	Male	Female
Disease	F349 IV.2 F349 IV.3 F349 V.1 F70 II.4 F436 II.1 F436 III.1 F432 II.3 F432 II.4 F432 II.5	F349 V.6 F70 II.8 F416 I.2 F32 III.1 F432 III.3
No disease	F349 V.3 F432 II.1 F432 II.6	F349.V.2 F70 II.3

1. Stuart, B.D., Choi, J., Zaidi, S., Xing, C., Holohan, B., Chen, R., Choi, M., Dharwadkar, P., Torres, F., Girod, C.E., et al. (2015). Exome sequencing links mutations in PARN and RTEL1 with familial pulmonary fibrosis and telomere shortening. Nat Genet 47, 512-517.

Supp. Table S2 Oligonucleotides used in this study

	5' -> 3'
[a]PARN^{ins} F primer	TGTTTGGGAAGATAGGCGCA
[a]PARN^{ins} R primer	CTCCTATGCATTTTTCAAGCAAGGC
[b]PARN^{Y91C} F primer for cDNA	CACAAAGTGTACCAGGCCATAGAG
[b]PARN^{Y91C} R primer for cDNA	TTCCTGATTTAAATATGGAATTCCATTTCG
[b]PARN^{Y91C} F primer for gDNA	TTGGAAGTATTCTGCTGAAGTCTCA
[b]PARN^{Y91C} R primer for gDNA	GGAGGAGATAACAGGGTCATGAATT
TERT promoter F primer	CGGGCTCCCAGTGGATTCGC
TERT promoter R primer	GACGCAGCGCTGCCTGAAAC
hTR F primer	TCTAACCCTAACTGAGAAGGGCGTAG
hTR R primer	GTTTGCTCTAGAATGAACGGTGGAAG
GAPDH F primer	CACATGGCCTCCAAGGAGTAAG
GAPDH R primer	TACATGACAAGGTGCGGCTCCC
PARN 5' UTR F primer	TTGGGGACTTCGATAGCCACGC
PARN 5' UTR R primer	GAGGCGCACCGGCTTAAGGA
PARN 3' UTR F primer	TGTTTTGTTCTTTCCCACCA
PARN 3' UTR R primer	AGTGTGAGTGCTAAGGGTCC
ITS1-59 probe	GCGGTGGGGGGGTGGGTGTG

[a]*PARN* c.819_820insTAGAAATCATTTCTAGAGTC (NM_002582.3)

[b]*PARN* c.272A>G (NM_002582.3)

Supp. Table S3 Telomere length measured by flow FISH in granulocytes and subpopulations of lymphocytes

Telomere lengths in kb and classification:
VL <1 percentile; L ≥ 1 and < 10 percentile; N ≥10 and <90 percentile; NSQ not sufficient quantity

ID Test #	Age	Lymphocytes			Granulocytes			CD45RA+ (Naïve T)			CD45RA- (Memory T)			CD20+ (B Cells)			CD57+ (NK Cells)		
proband #1	7 y	4.0	9.4	VL	4.9	9.9	VL	4.3	9.6	VL	3.4	8.6	VL	5.1	9.5	VL	3.5	9.3	VL
proband #2	13 y	4.4	8.6	VL	5.4	9.4	VL	4.9	9.1	VL	3.9	7.8	VL	5.6	9.0	VL	4.3	8.3	VL
proband #3	15 y	3.9	8.4	VL	4.7	9.2	VL	4.5	8.9	VL	3.2	7.5	VL	5.3	8.9	VL	3.7	8.0	VL
proband #4	16 y	3.8	8.3	VL	4.3	9.2	VL	4.4	8.8	VL	3.3	7.4	VL	5.6	8.8	VL	3.8	7.8	VL
proband #5	17 y	3.9	8.2	VL	4.8	9.1	VL	4.7	8.7	VL	3.1	7.3	VL	5.1	8.7	VL	3.7	7.7	VL
S1 #1	8 y	7.4	9.2	L	8.1	9.8	L	8.2	9.5	N	6.8	8.5	L	8.6	9.4	N	6.4	9.1	L
S1 #2	15 y	7.3	8.4	N	8.5	9.2	N	8.2	8.9	N	6.2	7.5	L	8.2	8.9	N	6.9	8.0	N
S2 #1	3 m	7.5	10.4	VL	6.9	10.7	VL	7.5	10.3	VL	7.4	10.0	VL	7.5	10.2	VL	NSQ		
S2 #2	10 m	7.0	10.2	VL	7.7	10.5	VL	7.1	10.2	VL	6.8	9.7	VL	7.2	10.1	VL	NSQ		
S2 #3	2 y 2 m	6.6	10.1	VL	NSQ			6.7	10.1	VL	6.4	9.5	VL	6.7	10.0	VL	5.9	10.3	VL
S2 #4	3 y 3 m	5.9	9.9	VL	5.8	10.3	VL	6.0	10.0	VL	5.7	9.4	VL	6.0	9.9	VL	5.5	10.1	VL
S2 #5	3 y 10 m	6.1	9.9	VL	6.3	10.3	VL	6.2	10.0	VL	5.7	9.4	VL	6.3	9.9	VL	5.4	10.1	VL
M #1	32 y	7.2	7.1	N	8.2	8.4	N	8.1	7.8	N	6.7	6.1	N	9.0	8.1	N	5.8	6.4	N
M #2	39 y	6.6	6.8	N	NSQ			6.8	7.4	N	6.0	5.9	N	8.9	7.9	N	4.5	6.0	N
F #1	33 y	5.0	7.1	L	6.0	8.4	L	5.5	7.7	L	4.6	6.1	L	6.6	8.0	L	3.2	6.3	L
F #2	41 y	5.5	6.7	L	6.7	8.2	L	6.5	7.3	N	4.3	5.8	L	6.5	7.8	L	5.1	6.0	N
GP1 #1	62 y	5.4	6.1	N	7.5	7.9	N	5.8	6.5	N	5.1	5.5	N	7.2	7.5	N	5.2	5.6	N
GP2 #1	60 y	6.3	6.1	N	8.2	7.9	N	6.6	6.6	N	5.9	5.5	N	8.3	7.5	N	4.6	5.6	N
GP3 #1	67 y	5.8	5.9	N	7.4	7.8	N	4.3	6.3	L	5.8	5.4	N	8.2	7.4	N	4.9	5.5	N
GP4 #1	66 y	4.8	5.9	N	6.0	7.8	L	4.1	6.3	L	4.9	5.4	N	7.2	7.5	N	4.3	5.5	N